UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,683	04/07/2006	Frieder Schwenk	100725-49 KGB	6034

27384 7590 03/10/2010

Briscoe, Kurt G.
Norris McLaughlin & Marcus, PA
875 Third Avenue, 8th Floor
New York, NY 10022

EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
03/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,683	SCHWENK ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-19,24,25,28-30,32-41 and 43-58* is/are pending in the application.

4a) Of the above claim(s) *47 and 49-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-19,24,25,28-30,32-41,43-46,48 and 53-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12-7-09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16, 20-23, 26, 27, 31, 42 have been canceled. Claims 57 and 58 have been added. Claims 17-19, 24, 25, 28-30, 32-41, 43-58 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 12-7-09 have been fully considered but they are not persuasive.

Election/Restrictions

Claims 47 and 49-52 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 1-28-08.

Claims 17-19, 24, 25, 28-30, 32-41, 43-46, 48 and 53-58 are under consideration.

Claim Rejections - 35 USC § 112

New Matter

Claims 17-19, 24, 25, 28-30, 32-41, 43-46, 48 and 53-56 remain and claims 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection of claim 17 regarding "wherein the promoter is heterologous to the Rosa26 locus" would have been withdrawn in view of pg 8, lines 1-2. However, the rejection has been withdrawn in view of amending the phrase to "Rosa26 gene."

Claim 17 is newly rejected under new matter because the specification does not teach or imply the phrase "Rosa26 gene" as now claimed. Support for the phrase cannot be found and applicants have not indicated why the phrase must be implicit from the "Rosa26 locus" described throughout the specification. The Rosa26 locus is a position on a chromosome while the gene has a structure and function. It is not readily apparent that the Rosa26 gene was implicit from the position of Rosa26 on a chromosome. Clarification is required.

Claim 17 remains new matter because the specification does not teach or suggest "a DNA sequence which can be converted into such gene expression cassette." Applicants have not argued this aspect of the rejection. Support for the phrase has not been provided and cannot be found in the specification as originally filed.

Claim 53 remains new matter. Support cannot be found for expressing a gene of interest and evaluating the function of the gene. Applicants point to pg 5, line 9-10, which teaches the transgenic can be used for gene function studies. Applicants point to original claim 16. Applicants generically state the steps are obvious from the intended use in the specification. Applicants' arguments are not persuasive. Pg 5 does not teach the steps of expressing a gene of interest and evaluating the function of the gene as claimed. Applicants have not explained why the specific steps of "expressing the gene of interest and (c) evaluating the function of the gene of interest" as claimed are

implicit from the suggestion of using cells for "gene function studies" in original claim 16. It is not readily apparent applicants contemplated the specific steps claimed.

Claim 54 remains new matter. Support cannot be found for "evaluating the effect of the drug candidate on the gene of interest." Applicants point to pg 5, line 9-10, which teaches the transgenic can be used for drug development. Applicants generically state the steps are obvious from the intended use in the specification. Applicants' arguments are not persuasive. Pg 5 does not teach the steps of contacting a drug candidate with a biological entity and evaluating the effect of the drug as claimed. Applicants have not explained why using cells for "evaluating the effect of the drug candidate on the gene of interest" as claimed is implicit from the suggestion of using transgenic for drug development on pg 5. It is not readily apparent applicants contemplated the specific steps claimed.

Claim 55 remains new matter. Support cannot be found for providing an animal model of disease, "expression of the gene of interest models a disease state of said animal", contacting a "biological entity" with a drug candidate, and evaluating the effect of the drug on the gene of interest. Applicants point to pg 5, line 9-10, which teaches the transgenic can be used as disease model animals. Applicants generically state the steps are obvious from the intended use in the specification. Applicants' arguments are not persuasive. Pg 5 does not teach using models of disease to test drugs or "expression of a gene of interest models a disease state." Applicants have not explained why the steps claimed are implicit from the suggestion of using transgenics

as a disease model. It is not readily apparent applicants contemplated the specific steps claimed.

Claim 56, step b), remains new matter. Applicants again point to the pg 9, last three lines, which state: "a donor DNA comprising the same two mutually incompatible first RRSs contained in the acceptor DNA by utilizing a recombination vector as defined above". Applicants' argument is not persuasive. Step b) requires "(b) introducing a recombination vector comprising a functional DNA sequence into the acceptor DNA-modified eukaryotic cell, the functional DNA sequence in the recombination vector being donor DNA flanked by two mutually incompatible RRSs that are identical to the two mutually incompatible RRSs in the acceptor DNA". Pg 9 does not contemplate a recombination vector comprising a "functional DNA sequence", that the two RSSs "flank" the donor DNA or that the two RSSs are identical to the RSSs of step a) as claimed.

Support for new claim 57 is found in claim 35.

Support for new claim 58 is found in claim 46.

Applicants' responses should always begin with a section describing where support comes for each new phrase or new claim added in an amendment.

Indefiniteness

Claims 32, 33, 43-45, 55, 56 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 17 regarding "modified Rosa26 locus" has been withdrawn because the phrase has been changed to "modified Rosa26 gene."

The rejection of claim 19 regarding the phrase "site specific recombinase mediated recombination" has been withdrawn in view of Craig (1998) in the IDS filed 12-07-09.

The rejection of claim 28 regarding the metes and bounds of "primary" has been withdrawn in view of applicants' arguments regarding Watson (1988).

The rejection of claim 30 regarding the phrase "pharmaceutically active proteins and peptides" has been withdrawn in view of applicants' arguments.

The metes and bounds of what applicants consider an "inducible ubiquitous promoter" and "inducible tissue specific promoter" in claim 32 remain indefinite. The structure of such promoters is not defined in the specification or the art at the time of filing. Applicants argue the phrases are well known promoter genera and species. Applicants point to the first paragraph on pg 8. Applicants' argument is not persuasive. Applicants' argument regarding the art at the time of filing is unfounded. Furthermore, the art at the time of filing did not define which promoters are "inducible ubiquitous promoters" and "inducible tissue specific promoters". Without a definition, those of skill would not know when they were infringing on the claim. Applicants point to Kuhn, who taught inducible promoters, and the list of promoters on pg 8, which generically lists numerous promoters. Applicants' arguments are not persuasive. While the Mx1 promoter may be inducible, it is not readily apparent that the Mx1 promoter is "an inducible ubiquitous" promoter as claimed. Nor does the list on pg 8 of the specification

define which promoters are "inducible ubiquitous" or "inducible tissue specific" as claimed.

The metes and bounds of what applicants consider a "CAGGS, hCMV, PGK, FABP, Lck, CamKII, CD19... ...aP2... ...MCK, MyHC, WAP, Col2A, Mx, tet and trex" promoter in claim 33 remain indefinite. The structure of such promoters is not defined in the specification or the art at the time of filing. Applicants argue the phrases are well known promoter genera and species. Applicants point to the first paragraph on pg 8. Applicants' argument is not persuasive. Applicants' argument regarding the art at the time of filing is unfounded. Furthermore, the art does not teach what the abbreviations stand for. The abbreviations should be spelled out where necessary or applicants should point to the definition of such abbreviations in the specification or the art at the time of filing. Applicants point to Table 1 from Torres (1997), which does not correlate to the list of promoters in claim 33. Nor does the Table define the structure or function of the promoters. Applicants have only provided the Table without providing the reference as a whole which has citations for some of the promoters in claim 33. In addition, the promoters claimed are still abbreviated. Therefore, those of skill would not be able to determine when they were infringing on the claim.

The rejection of claim 35 has been withdrawn in view of the amendment.

Claim 45 remains indefinite because it is unclear what applicants consider an "inactive" positive selection marker. Applicants point to pg 10, section (iii) which uses the phrase and states neomycin phosphotransferase is an example. Applicants argue the markers were known to those of skill in the art at the time of filing. Applicants'

arguments are not persuasive. Applicants' argument regarding the art at the time of filing is unfounded. The phrase was not defined by applicants or those of skill in the art at the time of filing. Giving one example is not enough for those of skill to determine the metes and bounds of the phrase. Therefore, those of skill would not know when they were infringing on the claim.

The rejection of claim 46 has been withdrawn in view of the amendment.

The rejection of claim 48 has been withdrawn in view of the amendment.

The rejection of claims 53-55 regarding providing a eukaryotic cell, a transgenic multi-cell non-human organism or a transgenic non-human mammal using the method of claim 17 has been withdrawn in view of the amendment.

The rejection of claims 53-55 regarding a cell, organism or mammal "obtainable utilizing the method of claim 17" has been withdrawn in view of the amendment.

The rejection of claims 54 and 55 regarding steps for "drug development" have been withdrawn in view of the amendment filed 6-30-09.

Claim 55 remain indefinite because it is unclear how an animal comprising a cell made by the method of claim 17 is a model of an animal disease. The claim encompasses an animal having one cell made by the method of claim 17, which cannot be a model of disease. Accordingly, there is no nexus between an animal with a cell made by claim 17 as broadly claimed and "models of disease."

Claim 56 remains indefinite because the metes and bounds of what applicants consider "two mutually incompatible RRSs" does not clearly set forth the structure or function of the acceptor DNA. Pg 9 uses the phrase (last 5 lines) and pg 10, first four

lines, use the term RSS, but the metes and bounds the phrase are unclear. Using the phrase does not mean the phrase is defined. Applicants have not disclosed the structure or function of "two mutually incompatible RRSs" on pg 9, 10 or any where else in the specification. Without such guidance, those of skill would not know when they were infringing on the claim. Claims 43-45 are included because they are dependent upon claim 56.

Claim Rejections - 35 USC § 102

Claims 17-25, 28-30, 32-32, 34-38, 43-46, 48 and 53-56 remain rejected under 35 U.S.C. 102(b) as being anticipated by Soprano (WO99/53017) for reasons of record.

Soriano made a Rosa26 transgenic mouse by introducing a DNA cassette comprising a LacZ gene flanked by loxP sites into the Rosa26 locus of a mouse ES cell and implanting the ES cell into a mouse blastocyst. The LacZ gene was under the control of the mouse Rosa26 promoter (Example 1, pg 30). Soriano also taught making a Rosa26Cre transgenic mouse (Example 2, pg 41) by introducing a construct into ES cells, the construct comprising a deletor cassette comprising a recombinase gene operably linked to an upstream splice acceptor (SA and a downstream polyA sequence with a positive selection cassette comprising a PGK promoter, the neo gene and a polyadenylation sequence (pg 7, lines 2-10). The construct was inserted into the targeting vector comprising homology arms for the Rosa26 gene and a diphtheria toxin gene for negative selection (pg 7, line 9-10; pg 7, line 1-2). Soriano also made a transgenic mouse by introducing a targeting vector into mouse ES cells, the vector comprising a reporter cassette comprising a splice acceptor operably linked to stuffer

DNA flanked by two loxP sites (pg 7, lines 10-16); the stuffer DNA comprised a PGK promoter, the neo gene and four polyA sites (pg 44, Example 3). The coding sequence described by Soriano is a "DNA sequence which can be converted into such gene expression cassette."

The cassette comprises a gene of interest operably linked to a PGK promoter (Fig. 1C; Fig. 4), which is "heterologous to the Rosa26 gene" as claimed. In the alternative, Soriano taught numerous Rosa26 promoter fragments including mutagenized promoters, (pg 34-35) which are "heterologous" as claimed because they are different in structure (especially the mutagenized Rosa26 promoter) than the original Rosa26 promoter (Heterologous is defined as "differing in structure and origin: describes organisms or parts that differ from each other in structure or origin" (Encarta Dictionary definition of "heterologous", 2010)). In a third alternative, Soriano taught "isogenic homology regions flank the exogenous targeting construct sequence that is to replace the targeted promoter gene locus sequence" (pg 26, lines 1-3, emphasis added), i.e. to replace the Rosa26 promoter with a heterologous promoter via recombination, which is equivalent to a promoter that is "heterologous to the Rosa26 gene" as claimed.

Applicants argue the customary definition of "heterologous" connotes being from another species. Applicants' argument is not persuasive. "Heterologous" means being from another tissue (Dorland Medical Dictionary definition of "heterologous", 2010) or "differing in structure and origin: describes organisms or parts that differ from each other

in structure or origin" (Encarta Dictionary definition of "heterologous", 2010). "Heterologous" is not limited to "xenogeneic" (which means from another species).

Applicants argue Rosa26 promoter fragments are not heterologous as claimed because they are still from the Rosa26 gene. Applicants' argument is not persuasive. The Rosa26 promoter fragments included mutagenized promoters, (pg 34-35) which they have a different structure than the original Rosa26 promoter. Heterologous is defined as "differing in structure and origin: describes organisms or parts that differ from each other in structure or origin" (Encarta Dictionary definition of "heterologous", 2010).

Applicants argue Soriano did not teach the promoter was heterologous to the ROsa26 locus. Applicants' argument is not persuasive. The cassette comprises a gene of interest operably linked to a PGK promoter (Fig. 1C; Fig. 4), which is "heterologous to the Rosa26 gene" as claimed. Soriano also taught "isogenic homology regions flank the exogenous targeting construct sequence that is to replace the targeted promoter gene locus sequence" (pg 26, lines 1-3), i.e. to replace the Rosa26 promoter with a heterologous promoter using recombination, which is equivalent to a promoter that is "heterologous to the Rosa26 gene" as claimed.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Primary Patent Examiner